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EXAMINER	
HAYES, ROBERT CLINTON	
ART UNIT	**PAPER NUMBER**
1647	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/956,518	Applicant(s) Leonard et al
	Examiner Robert C. Hayes, Ph.D.	Art Unit 1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 13, 2003*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 3-8, and 26-28* is/are pending in the application.

4a) Of the above, claim(s) *28* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 3-8, 26, and 27* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1, 3-8, and 26-28* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of SEQ ID NO: 94 for Group I (claims 1 & 3-8) in Paper No. 15 is acknowledged. The traversal is on the ground(s) that "the search and examination of the claimed invention would not constitute on (*sic*) undue burden on the Examiner, as all of the claimed SEQ ID NOS are portions of a *single* gene, the human alpha 7 neuronal nicotinic receptor". This is not found persuasive because each sequence is unique, as illustrated by each unique disclosed SEQ ID NO, and in which the full human alpha 7 neuronal nicotinic receptor gene sequence is not provided, which therefore, would create an undue burden on the Examiner to search and examine each and every otherwise unique sequence. *In arguendo*, the Sequence Rules in 37 CFR 1.822(o) state that a sequence made up of *one or more noncontiguous segments* of a larger sequence or segments from different sequences shall be presented as a separate sequence (i.e., as it relates to claim 28). In other words, because these "portions" are not from a single "disclosed" sequence, Applicants' arguments are not persuasive. It is noted that the claims directed toward other SEQ ID NOs have now been cancelled or amended to recite only SEQ ID NO: 94 (except for new claim 28, which therefore, is a nonelected invention). Note further that the mere reference to "GenBank #U40583" on page 63 of the specification was not incorporated by reference, which further would have been an improper incorporation by reference because a GenBank citation is not a U.S. patent. The requirement is still deemed proper and is therefore made FINAL.

Claim 28 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 15.

Information Disclosure Statement

2. The information disclosure statement filed 4/2/99 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. Note that Applicants are encouraged to use a PTO 1449.

Claim Rejections - 35 U.S.C. § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 6-8 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. For example, the current recitation in claim 8 of "A first polynucleotide sequence... comprising..." encompasses all naturally occurring DNAs; thereby, not involving the hand of man to isolate or purify the DNA. It is suggested that amending claim 8 to "an <u>isolated</u> first polynucleotide" should obviate the rejection of claim 8.

Additionally, the current recitation of "A host cell" encompasses a human organism. It is suggested that amending the claims to "an isolated host cell" should obviate the rejection of claims 6-7.

Claim Rejections - 35 U.S.C. § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In contrast to Applicants' assertions on page 7 of the response, no proper antecedent basis nor conception in context with that disclosed on page 71 of the specification exists for the broader recited "stringent" hybridization conditions which do not contain "0.05% SDS, 6X SSC and 50% formamide", which alternatively affects the melting temperature and, therefore, the stringency of the hybridization conditions; thereby, constituting new matter.

5. Claims 1, 3-8 & 26-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey

to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant specification discloses various small portions of the genomic DNA sequence for the human alpha-7 nicotinic receptor, which includes part of the promoter sequence depicted as nucleotides 1-392 of SEQ ID NO: 94 (see Figure 4). Although small portions of various splice junction sites of the human alpha 7 neuronal nicotinic receptor are also described, no written description of the complete human alpha-7 nicotinic receptor nucleic acid sequence is disclosed. Likewise, only the specific species of exon 1 and the corresponding splice donor of the human alpha 7 neuronal nicotinic receptor as set forth as nucleotides 393-457 of SEQ ID NO: 94 is described, versus any different putative generic sequence, or allelic variant thereof (i.e., as it relates to claims 26 & 27). In other words, no written description is provided in the instant specification as to what structurally constitutes nucleotide sequences "comprising" unknown and undescribed promoter sequences, 5'- or 3'-flanking or enhancer or silencer regions, "intervening regions", other "exon 1" or "intron 1 splice donor" sequences, or any other undescribed genomic sequence that "comprises" "nucleotides 1-392 of SEQ ID NO: 94", in that no sequences for these different molecules are described; nor can they be reasonably visualized by one skilled in the art (i.e. as it especially relates to claims 1, 3 & 4).

Second, in regards to hybridization products resulting in a "first polynucleotide sequence comprising at least fifteen nucleotides", the genus of such DNA promoter sequences, as currently claimed, encompass generic 5'-, 3'-flanking, enhancer, silencer, and additional promoter

sequences, which alternatively would be expected by the skilled artisan to have widely divergent functional properties. In contrast, the instant specification solely describes the human alpha-7 neuronal nicotinic receptor promoter as set forth as nucleotides 1-392 of SEQ ID NO: 94, in which no other promoter sequences are described. Therefore, one skilled in the art can not reasonably visualize or predict what critical nucleotide residues would structurally characterize a functional genus of polynucleotides that merely hybridize to the human alpha-7 neuronal nicotinic receptor as set forth as nucleotides 1-392 of SEQ ID NO: 94 (i.e., as it especially relates to claim 8); thereby, also not reasonably meeting the written description requirements under 35 U.S.C. 112, first paragraph.

It is suggested that amending the claims to "an isolated DNA molecule [comprising] consisting of ...nucleotides 1-392 of SEQ ID NO: 94" or "consisting of... SEQ ID NO: 94" should obviate this particular rejection.

Applicant is directed toward the Revised Interim Written description Guidelines, Federal Register, Vol.64, No.244, pages 71427-71440, Tuesday December 21, 1999 (e.g., see Examples 6, 7, 9 & 11).

6. Claims 1, 3-8 & 26-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific disclosed promoter nucleotide sequence of nucleotides 1-392 of SEQ ID NO: 94 for the human alpha-7 nicotinic receptor gene, does not reasonably provide enablement for any "portions" of nucleic acid molecule not encoding a

functional alpha-7 nicotinic receptor protein, or nonfunctional promoters, or fragments of exon/intron boundaries with no function. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The name "nucleotide sequence comprising a portion of the human alpha-7 neuronal nicotinic receptor", or "first polynucleotide sequence" which is merely a hybridization product thereof, does not sufficiently characterize and enable the polynucleotides that are encompassed by the claims, because the inclusion of other unknown and undescribed sequences (i.e., "comprising" "5' or 3' flanking regions", "intervening regions", altered promoter sequences that hybridize, etc.) or "comprising" incomplete sequences of a human alpha-7 neuronal nicotinic receptor sets forth little structural and little functional characteristics. In contrast, the specification does not teach what critical nucleotides are involved in appropriate human alpha-7 neuronal nicotinic receptor promoter function, nor what encoded particular amino acids are critical for any alpha-7 nicotinic receptor protein's function that are encoded by polynucleotides that "comprise exon 1" (i.e., as it relates to claims 1-3, 8 or 26-27). Nor does the specification teach how to distinguish any altered promoter sequence that is merely a hybridization product "comprising at least fifteen nucleotides" from any different nucleic acid molecule that possesses none of the desired functions of the instant invention. It should be noted that a nucleic acid sequence that merely hybridizes to "at least 15 nucleotides' of a putative alpha-7 nicotinic receptor nucleic acid sequence does not necessarily possess the desired properties of a human

alpha-7 nicotinic receptor molecule, without further structural and functional characterization to distinguish hybridization products with alpha-7 nicotinic receptor activity from any different molecule without alpha-7 nicotinic receptor gene activity (i.e., as it relates especially to claim 8). Alternatively, any "modification" to the disclosed human promoter sequence of nucleotides 1-392 of SEQ ID NO: 94 would reasonably be expected by the skilled artisan to either eliminate expression of the species/cell-specific expression of the human alpha-7 neuronal nicotinic receptor protein, or alter its expression pattern such that one could not distinguish the resultant expression pattern from a normal expression pattern; especially when no assayable function for determining how to make and use such altered molecules is provided within the specification. For example, page 26 of the specification states that "[t]he nucleotide sequence between the human and chick promoter regions was found to *not be well conserved* [emphasis added]". Additionally, LeClerc et al. (1982) teach random mutations to promoter sequences normally result in either an altered or inactive promoter sequence. Thus, the lack of guidance within the specification as to what critical nucleotides are involved in appropriate human alpha-7 neuronal nicotinic receptor promoter function would prevent one skilled in the art at the time of filing Applicants' invention to reasonably determine what alterations would constitute a functional invention, without requiring undue experimentation to discover how to make and use Applicants' invention.

Second, the skilled artisan would also reasonably expect that any random mutations, truncations or additions to a nucleic acid normally encoding an alpha-7 nicotinic receptor-related

molecule (e.g., encoding only exon 1; as it relates to claims 26 & 27) would result in a polynucleotide encoding an inactive protein. For example, Rudinger states on page 3 that "it is impossible to attach a unique significance to any residue in a sequence. A given amino acid will not by any means have the same significance in different peptide sequences, or even in different positions of the same sequence". Rudinger further states on page 6 that "the significance of particular amino acid sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study". Therefore, the lack of guidance provided in the specification, as to what minimal structural requirements are necessary for a nucleic acid to encode a functional alpha-7 nicotinic receptor molecule would prevent the skilled artisan from determining whether any random mutations/additions/truncations to human alpha-7 nicotinic receptor DNA molecule could be made that retains the desired function of the instant invention, because any such polynucleotide would be expected by to encode proteins that have adversely altered their biologically active 3-dimensional conformation, even though such molecules may be still hybridizable under stringent conditions, without undue experimentation to determine otherwise.

7. Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

No proper antecedent basis exists for the recitation of "mammalian cells" in the Markush group recitation in claim 7 for "said cell". It is suggested that amending the claim to "consisting of a bacteria, yeast, amphibian, and a mammalian cell[s]" would obviate this particular rejection.

8. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Only hybridization to the "fully complementary strand" of a "second polynucleotide sequence" would possibly produce an appropriate "first polynucleotide" sense strand that encodes an alpha-7 nicotinic receptor polypeptide, versus the noncoding antisense strand, as currently claimed; thereby, making it ambiguous what Applicants intended to claim.

Claim Rejections - 35 U.S.C. § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b).

Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claim 8 is rejected under 35 U.S.C. 102(e) as being anticipated by Elliott et al (U.S. Patent 5,837,489).

Elliott et al. teach the human alpha 7 neuronal nicotinic receptor cDNA sequence (i.e., SEQ ID NO: 7; cols.7 & 45-48), which comprises residue #s 321-447 of SEQ ID NO: 94, as well as exon 1 and the intron 1 splice donor site of the human alpha 7 neuronal nicotinic receptor (i.e., "at least fifteen nucleotides"; as it relates to claims 1, 26 & 27). However, Elliott et al do not teach the complete sequence depicted as SEQ ID NO: 94. Nevertheless, because residue #s 1-127 of Elliott's polynucleotide would hybridize under stringent conditions to 100% of the complementary sequence residue #s 321-447 of SEQ ID NO: 94, the limitations of claim 8 are clearly anticipated.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 872-9306. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

RCH

Robert C. Hayes, Ph.D.
September 26, 2003